IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Carter *et al.*	Confirmation No.:	8478
Patent No.:	7,642,228 B2	Art Unit:	1649
Issued:	January 5, 2010		
Application No.:	10/010,245	Examiner:	Gucker, Stephen
Filed:	December 7, 2001		
For:	METHOD FOR MAKING HETEROMULTIMERIC POLYPEPTIDES	Attorney Docket No.:	12279-493-999

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 C.F.R. § 1.322

Attention: Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Patentee hereby requests the issuance of a Certificate of Correction in connection with the above-identified patent. Please find the errors, as they appear in the patent, in the form PTO/SB/44 submitted herewith, as follows:

In claim 1, col. 38, line19, "iterface" should be replaced with -- interface--.

In claim 1, col. 38, lines 26-27, "polypeptide interface via a CH3 constant damain of an antibody" should be replaced with -- the first and second polypeptide interface via a CH3 domain of an antibody--.

In claim 7, col. 38, line 39, "armine" should be replaced with --arginine--.

The errors are of a clerical and typographical nature and incurred through the fault of the United States Patent and Trademark Office ("USPTO"). Patentee respectfully submits that the intended claim language of claims 1 and 7 is clearly disclosed in the records of the USPTO, in connection with U.S. Application No. 10/010,245, and hereby submits the following supporting documentation: (1) the Amendment and Response to Office Action, dated March 24, 2009 (Exhibit 1); and (2) the Notice of Allowability and Examiner's Amendment, dated August 20, 2009 (Exhibit 2).

Since the above-mentioned errors were incurred through the fault of the USPTO, it is estimated that no fee is due in connection with this request. However, should fees be necessary, please charge the required fee to Jones Day Deposit Account No. 50-3013. Please issue a Certificate of Correction in due course.

Respectfully submitted,

Date: February 5, 2010

59,672
Wayne Szeto (Reg. No.)
For: Steven X. Cui (Reg. No. 44,637)

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222 East 41st Street
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PTO/SB/44 (09-07)
Approved for use through 08/31/2010. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 7,642,228 B2

APPLICATION NO.: 10/010,245

ISSUE DATE : January 5, 2010

INVENTOR(S) : Paul J. Carter, Leonard G. Presta and John Ridgway

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In claim 1, col. 38, line19, "iterface" should be replaced with -- interface--.

In claim 1, col. 38, lines 26-27, "polypeptide interface via a CH3 constant damain of an antibody" should be replaced with -- the first and second polypeptide interface via a CH3 domain of an antibody--.

In claim 7, col. 38, line 39, "armine" should be replaced with --arginine--.

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Exhibit 1:

**Amendment and Response to Office Action,
dated March 24, 2009, for U.S. Patent Application No. 10/010,245**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	)	Examiner: Stephen Gucker
Paul J. Carter	)	Art Unit: 1645
Application Serial No. 10/010,245	)	Confirmation No. 8478
Filed: December 7, 2001	)	Attorney's Docket No. GNE-0321C2 (P0927C2)
For: **METHOD FOR MAKING HETEROMULTIMERIC POLYPEPTIDES**	)	**Customer No. 77845**

FILED VIA EFS – MARCH 24, 2009

AMENDMENT AND RESPONSE TO OFFICE ACTION

MAIL STOP: Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This paper is being filed in response to the Office Action mailed on October 2, 2008. It is being timely filed by April 2, 2009 with a request for a three (3) month extension of time and the requisite fee.

Pending Claims begin on page **2** of this paper.

Remarks/Arguments begin on page **7** of this paper.

Amendments to the Claims:

This listing of claims replaces all previous versions, and listings, of claims pending in this application:

1-24. (Canceled)

25. (Currently amended) An isolated heteromultimer comprising at least a first polypeptide and a second polypeptide, wherein

1) the first polypeptide is associated with the second polypeptide via an interface, said interface having introduced therein at least one protuberance or cavity such that ~~which meet at an engineered interface, wherein said engineered interface further comprises an interface of the first polypeptide, and an interface of the second polypeptide~~:

(a) the interface of the first polypeptide comprises a protuberance that is positionable in a cavity in the interface of the second polypeptide, or

(b) the interface of the first polypeptide comprises a cavity that accommodates ~~is positionable in~~ a protuberance of the second polypeptide,

~~wherein the protuberance or cavity, or both, have been introduced into the engineered interface~~ such that a greater ratio of heteromultimer:homomultimer forms than for a multimer having a wild-type ~~non-engineered~~ interface, and

2) the first and second polypeptides each comprise an antibody constant domain.

26-27. (Canceled)

28. (Previously presented). A composition comprising the heteromultimer of any of claims 25, 39, 57-59, 66, 75, and 81 and a pharmaceutically acceptable carrier.

29-38. (Canceled)

39 (Previously presented). The heteromultimer of Claim 25 wherein the interface comprises both (a) and (b).

40-41. (Canceled)

42. (Currently amended) The heteromultimer of Claim 25 wherein the protuberance has been introduced into the ~~engineered~~ interface.

43. (Currently amended) The heteromultimer of Claim 25 wherein the cavity has been introduced into the ~~engineered~~ interface.

44 (Previously presented) The heteromultimer of Claim 42, wherein protuberance comprises a non-naturally occurring amino acid residue.

45. (Previously presented) The heteromultimer of Claim 42, wherein the protuberance comprises a naturally occurring amino acid residue.

46. (Previously presented) The heteromultimer of Claim 45, wherein the protuberance comprises an arginine (R) residue.

47. (Previously presented) The heteromultimer of Claim 45, wherein the protuberance comprises a phenylalanine (F) residue.

48 (Previously presented). The heteromultimer of Claim 45, wherein the protuberance comprises a tyrosine (Y) residue.

49 (Previously presented). The heteromultimer of Claim 45, wherein the protuberance comprises a tryptophan (W) residue.

50 (Previously presented). The heteromultimer of Claim 42, wherein the cavity comprises a non-naturally occurring amino acid residue.

51 (Previously presented). The heteromultimer of Claim 42, wherein the cavity comprises a naturally occurring amino acid residue.

52 (Previously presented). The heteromultimer of Claim 51, wherein the cavity comprises an alanine (A) residue.

53 (Previously presented). The heteromultimer of Claim 51, wherein the cavity comprises a serine (S) residue.

54 (Previously presented). The heteromultimer of Claim 51, wherein the cavity comprises a threonine (T) residue.

55 (Previously presented). The heteromultimer of Claim 51, wherein the cavity comprises a valine (V) residue.

56. (Canceled)

57. (Currently amended) The heteromultimer of Claim 25, wherein the antibody constant domain ~~engineered interface~~ comprises an immunoglobulin constant domain.

58 (Previously presented). The heteromultimer of Claim 57, wherein the immunoglobulin constant domain is a CH3 domain.

59 (Previously presented). The heteromultimer of Claim 58, wherein the CH3 domain is from an IgG.

60 (Previously presented). The heteromultimer of Claim 59, wherein the IgG is of the IgG1 subtype.

61 (Previously presented). The heteromultimer of Claim 59, wherein the IgG is of the IgG2 subtype.

62 (Previously presented). The heteromultimer of Claim 59, wherein the IgG is of the IgG2A subtype.

63 (Previously presented). The heteromultimer of Claim 59, wherein the IgG is of the IgG2B subtype.

64 (Previously presented). The heteromultimer of Claim 59, wherein the IgG is of the IgG3 subtype.

65 (Previously presented). The heteromultimer of Claim 59, wherein the IgG is of the IgG4 subtype.

66 (Previously presented). The heteromultimer of Claim 25, wherein the first or second polypeptide further comprises a binding domain.

67 (Previously presented). The heteromultimer of Claim 66, wherein the binding domain is an antigen binding domain.

68 (Previously presented). The heteromultimer of Claim 66, wherein the binding domain is a ligand binding domain.

69 (Previously presented). The heteromultimer of Claim 66, wherein the binding domain is a receptor binding domain.

70 (Previously presented). The heteromultimer of Claim 66, wherein the binding domain is an enzymatic domain.

71 (Previously presented). The heteromultimer of Claim 66, wherein the binding domain is an antibody variable domain.

72 (Previously presented). The heteromultimer of Claim 25 which is a multi-specific antibody.

73 (Previously presented). The heteromultimer of Claim 72 which is a bi-specific antibody.

74 (Previously presented). The heteromultimer of Claim 72 which is a tri-specific antibody.

75 (Previously presented). The heteromultimer of Claim 25 which is an immunoadhesin.

76 (Previously presented). The heteromultimer of Claim 75 which is a multi-specific immunoadhesin.

77 (Previously presented). The heteromultimer of Claim 76 which is a bi-specific immunoadhesin.

78 (Previously presented). The heteromultimer of Claim 76 which is a heterodimer.

79 (Previously presented). The heteromultimer of Claim 76 which is a heterotrimer.

80 (Previously presented). The heteromultimer of Claim 76 which is a heterotetramer.

81 (Previously presented). The heteromultimer of Claim 25 which is an antibody-immunoadhesin chimera.

REMARKS

Claims 25, 28, 39, 42-55, and 57-81 are pending. Claims 25, 42-43, and 57 have been amended and support can be found throughout the specification and claims as originally filed, including for example at page 9, lines 18-19 and page 21, lines 13-15.

With respect to all claims, Applicants have not dedicated, disclaimed, or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Double Patenting

The Examiner has provisionally rejected claims 25, 28, 39, 42-55, and 57-81 on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 24-28 and 52-100 of copending Application No. 11/533,709. Applicants respectfully request that the Examiner hold this rejection in abeyance until notice of allowable subject matter.

Rejection under 35 U.S.C. §112, first paragraph – Written description

Claims 25, 28, 39, 42-55, and 57-81 have been rejected under 35 U.S.C. §112 as allegedly failing to comply with the written description requirement. The Examiner alleges that both

> the specification (pages 35-36) and the art indicate that in order to produce heteromultimers that meet the limitations of the claims, the three-dimensional structure of the heteromultimer must be known down to the resolution of individual atoms by such techniques as X-ray crystallography, and determining the geometrical fitting of two (or more) polypeptide molecules in a protein-protein interaction is exceedingly complex and requires the knowledge of using pairs of critical points in combination with an adequate description of the respective molecular surfaces of the two polypeptides (Norel *et al.*, page 933; see also Figure 1). [emphasis added] (*Id.* at pages 4-5).

In addition, the Examiner states that

> one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by members of the genus, because the pairing of only 4 specifically numbered amino acid positions in the C_H3 antibody constant domain region is not representative of the claimed genus. (page 5 of the October 2, 2008 Office Action)

Applicants respectfully disagree and submit that when the proper legal standard for the written description requirement is applied, the pending claims are in compliance with the requirement. As such, Applicants respectfully request reconsideration by the Examiner and a withdrawal of the rejection.

A. The Legal Test for Written Description

The well-established test for sufficiency of support under the written description requirement of 35 U.S.C. §112, first paragraph, is "whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language" (*In re Kaslow*, 707 F.2d 1366, 1374, 212 USPQ 1089, 1096 (Fed. Cir. 1983; S*ee also Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991). The adequacy of written description support is a factual issue and is to be determined on a case-by-case basis. (*See, e.g., Vas-Cath*, 935 F.2d at 1563; 19 USPQ2d at 1116). The factual determination in a written description analysis depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. *Union Oil v. Atlantic Richfield Co.*, 208 F.2d 989, 996 (Fed. Cir. 2000; *See also* M.P.E.P. §2163 II(A)).

With regard to biomolecules, M.P.E.P. §2163 II A. 3. (a) provides that the U.S. Court of Appeals for the Federal Circuit has explained that

> "(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must

contain a recitation of known structure." *Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006). See also *Capon v. Eshhar*, 418 F.3d at 1358, 76 USPQ2d at 1084 (Fed. Cir. 2005).

Furthermore, the Court in *Falkner* acknowledged that the recitation of known sequence information would not serve the purpose of the written description requirement and the "forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification" (*Falkner* 448 F.3d at 1368).

B. Application of the Legal Test for Written Description

As currently amended, claim 25 recite "wherein the first and second polypeptides each comprise an antibody constant domain". Applicants respectfully submit that when the legal standard described above is applied, it must be found that the disclosure of the instant specification reasonably conveys to a person of ordinary skill in the art that the Applicants had possession of the genus of heteromultimers recited by claim 25, as currently amended.

Support for the genus can be found in the instant specification and in the relevant scientific literature concerning three-dimensional nature of antibody constant domains at the time of filing. For example, figure 5 provides the interface residues for various antibody constant domains, including those suitable for manipulation to provide an engineered interface; Figure 6 provides interface residues for various antibody subtypes; and Figure 9 provides a three-dimensional depiction of the protein-protein interaction of a C_H3 dimer based upon the structure of human IgG1 Fc (Deisenhofer, *Biochem.* 20:2361 (1981)). The specification also provides well-known information about the side chain volumes for the amino acid residues in, for example, Table 1 on page 20, and protocols for practicing the present invention (pages 25-56 and the Examples).

Applicants submit that at the time of filing the public domain contained other reports concerning the three-dimensional structure of antibody constant domains. Submitted herewith, for example, are Thies *et al.*, *J Mol Biol.*, 1999 Oct 15;293(1):67-79 which used X-ray crystallography to analyze folding of an Ig C_H3 domain; and Jefferis *et*

al. Immunol Rev., 1998 Jun;163:59-76 that provides a review of the interaction sites in the Fc region of human Ig for effector ligands, including a discussion of the topographical distribution of ten such sites. As stated in *Falkner*, the recitation of such public information in the Applicants' specification would not serve the purpose of the written description requirement.

In addition, the authors of Norel *et al.* (cited by the Examiner) report that a simple and straightforward modification of a well-known matching algorithm using surface complementarity between receptor and ligand protein molecules was successful. (Abstract) For instance, the authors indicate that out of the "16 protein-protein complexes we have tried, 15 were successfully docked" and the "entire molecular surfaces were considered, with absolutely no additional information regarding the binding sites" (Abstract). Therefore, straight-forward and predictable protocols for examining protein-protein three-dimensional protein-protein interactions were likewise available.

Based on the specification and publically available scientific knowledge at the time of filing, a person of ordinary skill in the art could (i) utilize known three-dimensional structural information for antibody constant domains provided by the instant specification and in the public domain, (ii) introduce any necessary site-directed mutations in the amino acid sequence, (iii) express and obtain the antibody constant domains using established cell lines and protocols, in order to form the heteromultimers of the present invention. The three-dimensional structural information for antibody constant domains is well-known to those of ordinary skill in the art, and therefore need not be disclosed for purposes of supporting the genus contemplated by the currently pending claims.

Withdrawal is respectfully requested.

Rejection under 35 U.S.C. §112, second paragraph – Definiteness

The Examiner has rejected claims 25, 28, 39, 42-55, and 57-81 under 35 U.S.C. §112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention (page 6 of the October 2, 2008 Office Action). The Examiner asserts that the phrase "'greater ratio of heteromultimer: homomultimer forms than for a multimer' is vague and confusing since the terms homomultimer and multimer have no antecedent basis" (page 6 of the October 2, 2008 Office Action). Applicants respectfully disagree and traverse the rejection.

Applicants believe that the terms "a greater ratio of heteromultimer:homomultimer" and "multimer" do not require antecedent basis as each appears for the first time following the article "a". A person of ordinary skill in the art would appreciate that the term "multimer" means the association of two or more polypeptides (either the first or the second polypeptide) and the term "homomultimer" means the association of two or more of the same polypeptide (either the first or the second polypeptide). As such, Applicants submit that claim 25 and all claims depending therefrom are clear and definite. Applicants respectfully request the withdrawal of the rejection.

Rejection under 35 U.S.C. §102

The Examiner has rejected claims 25, 28, 42-43, 45-47, 51, 53-54, 66, and 68 under 35 U.S.C. §102 (a) as allegedly being anticipated by Zhang *et al.* (1994) *Mol. Cell. Biol.*, 14(6):4311-4323 (hereinafter referred to as "Zhang"). The Examiner has rejected claims 25, 28, 39, 42-43, 45-47, 51-55, 66-69, 71-73, 75-78, and 81 under 35 U.S.C. §102 (b) as allegedly being anticipated by Tso *et al.* WO 93/11162 (hereinafter referred to as "Tso") in light of Goodman *et al.* (1991) *Biochemistry*, 30:11615-11620 and Landschulz *et al.* (1988) *Science*, Jun 24, 1988: 240:1759-1764. Applicants respectfully disagree and traverse the rejection.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

As currently amended, claim 25 recites "wherein the first and second polypeptides each comprise an antibody constant domain". With regard to Zhang and Tso, Applicants submit that neither reference teaches or suggests this element. As neither Zhang nor Tso teach or suggest all the claims elements of pending claim 25, neither can anticipate claim 25, or any other claim depending therefrom. Therefore, Applicants respectfully request the withdrawal of the rejection.

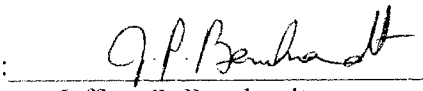
CONCLUSION

In light of the above amendments, Applicants believe that this application is now in condition for immediate allowance and respectfully request that the case be passed to issue.

Please charge any fees that might become applicable, including any fees for extension of time, or credit overpayment to Deposit Account No. 50-4634, referencing Attorney's Docket No. GNE-0321C2 (P0927C2) (123851-183886).

Respectfully submitted,
GOODWIN PROCTER LLP

Dated: March 24, 2009

By: 
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LIBC/3556247.1

Exhibit 2:

Notice of Allowability and Examiner's Amendment, dated August 20, 2009 for U.S. Patent Application No. 10/010,245

Notice of Allowability	Application No.	Applicant(s)	
	10/010,245	CARTER ET AL.	
	Examiner	Art Unit	
	STEPHEN GUCKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *3/24/09*.

2. ☒ The allowed claim(s) is/are *25,39,42-55,59-82, renumbered as 1-40 respectively*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 3/24/09
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee. Authorization for this examiner's amendment was given in a telephone interview with Jeffrey P. Bernhardt on 8/14/09.

An examiner's amendment to the record appears below.

In the specification:

Page 1, line 2: inserted after "1997,": --now abandoned,--.

In the claims:

Canceled claims 28 and 57-58.

In claim 25, line 9: changed "or" to --and/or--.

In claim 25, line 15, deleted "polypeptides each comprise an antibody constant domain."

In claim 25, line 15, inserted after "second":

--polypeptide interface via a CH3 constant domain of an antibody.--.

In claim 44, line 1: inserted after "wherein": --the--.

In claim 50, line 1: changed "42" to --43--.

In claim 51, line 1: changed "42" to --43--.

In claim 59, line 1: changed "58" to --25--.

Added new claim 82:

82. (New) A composition comprising the heteromultimer of any of claims 25, 39, 59, 66, 75, and 81 and a pharmaceutically acceptable carrier.

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is 571-272-0883. The examiner can normally be reached on Mondays through Fridays from 0930 to 1800.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/S. G./

Examiner, Art Unit 1649

Stephen Gucker

August 20, 2009

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649